

Modeling of Ionic Hydrogel Kinetics in Buffered Solutions

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ABSTRACT

In this paper, we present the meshless Finite Cloud Method (FCM) for the solution of a time-dependent partial differential equation governing ionic gel swelling. Using a point distribution, FCM constructs interpolation functions without assuming any connectivity between points. A collocation approach forces the unknowns at every point to satisfy the governing equation or boundary condition.

To validate the model, a cylindrical hydrogel was fabricated and subjected to step changes in solution pH to characterize the hydrogel's dynamic behavior. The hydrogel's equilibrium behavior was matched using a thermodynamic model. Numerical results show good agreement with experimental data.

Keywords: hydrogels, simulation, swelling, experiments, meshless method

1 INTRODUCTION

Ionic hydrogels are composed of a crosslinked polymer network containing ionizable groups immersed in an aqueous solution. Hydrogels are capable of undergoing large reversible deformations in response to changes in several environmental factors [1]. Hydrogel size is sensitive to solution pH, salt concentration, temperature, and electric fields. Special modification of the polymer's structure can also lead to gels that are sensitive to specific biological agents [2]. The properties of hydrogels have already been exploited in a number of applications including control of microfluidic flow, muscle-like actuators, filtration, separation, and drug delivery. To efficiently design and optimize hydrogel performance, accurate models of gel kinetics are needed. In this paper, we develop and solve a nonlinear chemical diffusion equation using the meshless Finite Cloud Method (FCM) to predict gel swelling/deswelling kinetics.

FCM is a meshless method based on a fixed kernel approximation. Interpolation functions are constructed from a point distribution that approximates the problem domain. No assumption of connectivity between the points is made. Using collocation, each point within the problem domain is forced to satisfy the governing

partial differential equation or an appropriate boundary condition.

Modeling gel kinetics requires accurately describing the diffusion of hydrogen into and out of the gel. This requires taking into account the chemical reactions of the hydrogen ions with the fixed charge groups and buffer's effect on hydrogen diffusion. The governing equation developed here modifies Grimshaw's equation for hydrogel kinetics to include the influences of pH buffer in the solution [3]. The time-dependent governing equation is linearized and solved by using the FCM in space and a forward difference in time. Results from the numerical model are compared to experimental swelling and deswelling experiments performed on a cylindrical hydrogel. Equilibrium data was fit using a thermodynamic model.

2 GOVERNING EQUATIONS

2.1 Equilibrium Model

Generally, thermodynamic models consider three contributions to the free energy of a crosslinked polymer-solvent system - polymer-solvent mixing, deformation of the polymer network, and the osmotic pressure due to mobile ions [4],[5]. Despite their simplicity, thermodynamic equilibrium models do not give good quantitative results [4],[6]. Many of the input parameters in the model are difficult to determine and are often adjusted to 'fit' the model to the gel's equilibrium behavior. However, qualitatively, these models perform well.

At equilibrium, the chemical potential of the solution inside and outside of the hydrogel is equal, and can be expressed as the sum of the ionic contribution $(\Delta\mu)_{ion}$, mixing contribution $(\Delta\mu)_{mix}$, and the polymer's elastic response $(\Delta\mu)_{el}$.

$$(\Delta\mu)_{ion} - (\Delta\bar{\mu})_{ion} = (\Delta\bar{\mu})_{mix} + (\Delta\bar{\mu})_{el} \quad (1)$$

The concentration difference of mobile ions inside the gel and in the outer bath leads to an osmotic pressure which tends to swell the gel. When the gel is placed in an aqueous solution of sodium chloride ($NaCl$), the

ionic contribution to chemical potential is

$$(\Delta\mu)_{ion} - (\Delta\bar{\mu})_{ion} = V_1 RT [(\bar{c}_H - c_H) + (\bar{c}_{Na} - c_{Na}) + (\bar{c}_{Cl} - c_{Cl})] \quad (2)$$

where V_1 is the molar volume of the surrounding solution, R is the universal gas constant, T is the temperature, c_H is the bath concentration of hydrogen, c_{Na} is the bath concentration of sodium, and c_{Cl} is the bath concentration of chlorine. \bar{c}_H , \bar{c}_{Na} , and \bar{c}_{Cl} are ion concentrations in the gel. Using Donnan partitioning theory, interior ion concentrations can be related to bath concentrations through the Donnan ratio, λ .

$$\lambda = \frac{\bar{c}_H}{c_H} = \frac{\bar{c}_K}{c_K} = \frac{c_{Cl}}{\bar{c}_{Cl}} \quad (3)$$

Mixing represents the polymer's tendency to surround itself with solution or remain separated. The chemical potential of mixing is given by

$$(\Delta\mu)_{mix} = RT [\ln(1 - \phi) + \phi + \chi\phi^2] \quad (4)$$

where χ is the Flory parameter which ranges from 0 to 1, and ϕ is the volume fraction of polymer.

From the statistical theory of rubber elasticity, the elastic contribution of the polymer network to the chemical potential can be calculated as [7]

$$(\Delta\mu)_{el} = RT \left(\frac{V_1}{\bar{\nu}\bar{M}_c} \right) \left(1 - \frac{2\bar{M}_c}{\bar{M}_n} \right) \phi_o \left[\left(\frac{\phi}{\phi_o} \right)^{\frac{1}{3}} - \frac{1}{2} \left(\frac{\phi}{\phi_o} \right) \right] \quad (5)$$

where $\bar{\nu}$ is the molar volume of the polymer, \bar{M}_c is the molecular weight of the polymer chain between crosslinks, \bar{M}_n is the average molecular weight of the polymer chains before crosslinking, and ϕ_o is the polymer volume fraction before swelling.

Substituting equations (2)-(5) into equation (1) gives

$$\begin{aligned} & -V_1 \left[(\lambda - 1)c_H + (\lambda - 1)c_K + \left(\frac{1}{\lambda} - 1 \right) c_{Cl} \right] \\ & + [\ln(1 - \phi) + \phi + \chi\phi^2] \\ & + \left(\frac{V_1}{\bar{\nu}\bar{M}_c} \right) \left(1 - \frac{2\bar{M}_c}{\bar{M}_n} \right) \phi_o \left[\left(\frac{\phi}{\phi_o} \right)^{\frac{1}{3}} - \frac{1}{2} \left(\frac{\phi}{\phi_o} \right) \right] = 0 \end{aligned} \quad (6)$$

Equation (6) contains two unknowns, ϕ and λ . Electroneutrality inside the gel provides an additional equation containing the same unknowns

$$- \left(\frac{\phi}{\phi_o} \right) \frac{\sigma_o K_a}{K_a + c_H} + \lambda c_H + \lambda c_K - \frac{1}{\lambda} c_{Cl} = 0 \quad (7)$$

where σ_o is the concentration of ionizable groups in the polymer before swelling, and K_a is the dissociation constant of the ionizable groups.

2.2 Kinetic Model

pH induced swelling of ionic hydrogels is a diffusion limited process, and can be modeled by only considering the diffusion of hydrogen ions in the hydrogel [3]. This approach assumes that the mechanical deformation of the polymer network occurs instantaneously compared to the diffusion of hydrogen. The presences of buffer in the solution increases the apparent diffusion rate of hydrogen by providing an alternate path for diffusing hydrogen ions into or out of the hydrogel. The conjugate base of the buffer reversibly binds hydrogen ions in regions of high concentration and releases the hydrogen after diffusing to a region of lower concentration [6]. Buffer augmented transport of hydrogen under certain conditions can result in apparent diffusion rates of hydrogen which are several orders of magnitude higher than the diffusion coefficient of hydrogen alone [8].

The buffer's effect on the transport of hydrogen can be modeled by including additional terms in the continuity equation of hydrogen in the gel [3]

$$\frac{\partial}{\partial t} (H\bar{c}_H + H\bar{c}_H^b + H\bar{c}_{HB}) = - \frac{\partial(\alpha\Gamma_H + \alpha\Gamma_{HB})}{\partial\psi} \quad (8)$$

where H is the gel's hydration (ratio of fluid to solid volume), \bar{c}_H is the internal concentration of hydrogen, \bar{c}_H^b is the concentration of hydrogen ions reversibly bound to the hydrogel's fixed charges, \bar{c}_{HB} is the concentration of hydrogen bound to the buffer, α is the total area of the hydrogel normalized to its initial area, ψ is the Lagrangian coordinate system associated with the hydrogel, Γ_H is the flux of hydrogen ions, and Γ_{HB} is the flux of the hydrogen bound to the buffer. Using a reaction isotherm, \bar{c}_{HB} can be expressed in terms of \bar{c}_H by

$$\bar{c}_{HB} = \frac{\bar{c}_T \bar{c}_H}{K_B + \bar{c}_H} \quad (9)$$

where K_B is the dissociation constant of the buffer and \bar{c}_T is the total buffer concentration given by $\bar{c}_T = \bar{c}_{B^-} + \bar{c}_{HB}$. \bar{c}_{B^-} represents the internal concentration of the buffer's conjugate base. The flux of hydrogen in absence of an electric field is

$$\Gamma_H = \frac{H}{1 + H} \left[-\bar{D}_H \frac{\partial\bar{c}_H}{\partial x} \right] \quad (10)$$

where \bar{D}_H is the diffusion rate of hydrogen in the hydrogel. The flux of the buffer is proportional to the flux of the hydrogen ions

$$\Gamma_{HB} = \frac{\bar{D}_{HB}}{\bar{D}_H} \frac{\bar{c}_T}{K_B + \bar{c}_H} \Gamma_H \quad (11)$$

where \bar{D}_{HB} is the diffusion rate of the buffer in the hy-

drogel. Using equations (9)-(11), equation (8) becomes

$$\frac{\partial}{\partial t} \left[H\bar{c}_H + \frac{\bar{c}_{mo}^s \bar{c}_H}{K + \bar{c}_H} + \frac{H\bar{c}_T \bar{c}_H}{K_B + \bar{c}_H} \right] = \frac{\partial}{\partial \psi} \left[\alpha \left(\frac{H}{1+H} \right) \left(1 + \frac{\bar{D}_{HB}}{\bar{D}_H} \frac{\bar{c}_T}{K_B + \bar{c}_H} \right) \left(\bar{D}_H \frac{\partial \bar{c}_H}{\partial x} \right) \right] \quad (12)$$

3 FINITE CLOUD METHOD

The interpolations functions employed by the FCM are based on a fixed kernel approximation [9]. This method uses a corrected kernel to generate an approximation $u^a(x)$ to some unknown function $u(x)$. The one-dimensional form of the approximation is expressed as

$$u^a(x) = \int_{\Omega} \bar{\omega}_d(x_K - s)u(s)ds \quad (13)$$

where Ω is the domain occupied by the gel and $\bar{\omega}_d(x_k - s)$ is the corrected kernel function given by

$$\bar{\omega}_d(x - s) = C(x, s)\omega_d(x_K - s) \quad (14)$$

$C(x, s)$ represents the correction function, $\omega_d(x_K - s)$ is the uncorrected kernel function, and x_K is any point in the domain where the kernel is centered. In discrete form, equation (13) can be written as

$$u^a(x) = \sum_{I=1}^{NP} N_I(x)u_I \quad (15)$$

where NP is the number of points in the domain, $N_I(x)$ is the interpolation function at node I , and u_I is the unknown nodal value associated with node I . The interpolation function $N_I(x)$ is defined as

$$N_I(x) = C(x, x_I)\omega_d(x_K - x_I)\Delta V_I \quad (16)$$

where ΔV_I is a measure of the domain surrounding point I . In this work, a cubic spline is used for the kernel function ω_d . Numerical solution of partial differential equations using the finite cloud method is discussed in detail in [9].

4 RESULTS

Cylindrical gels were fabricated using photopolymerization techniques within microchannels. The gels were composed of HEMA with acrylic acid embedded in the polymer chains. The rectangular cross section of the microchannel was approximately 1000 μm wide by 180 μm high. Because the microchannel constrains the hydrogel's height, the volume of the hydrogel is only a function of diameter. All diameter measurements were converted to hydration values.

Table 1: Equilibrium model parameters

\bar{M}_c	35 M.W.	ϕ_o	1.0
\bar{M}_n	75000 M.W.	pKa	$5.3 \frac{\text{mol}}{\text{L}}$
$\bar{\nu}$	$0.0008 \frac{\text{L}}{\text{g}}$	σ_o	$63 \frac{\text{mol}}{\text{L}}$
V_1	$0.018 \frac{\text{L}}{\text{mol}}$	χ	0.49
C_{Cl}	0.2 M	C_{Na}	0.2 M

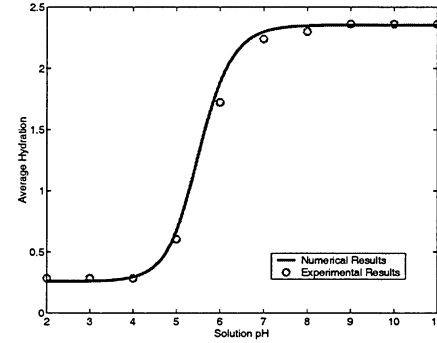


Figure 1: Comparison of numerical and equilibrium swelling

4.1 Equilibrium Results

The equilibrium behavior of the gel was characterized by varying the pH of the solution and measuring the equilibrium diameter of the cylinder using a microscope with a built-in ruler. The hydrogel's equilibrium size with respect to solution pH was fit using equations (6) and (7). A Newton method was used to solve for ϕ and λ . Numerical parameters used in the model are given in Table 1. For the chosen parameters, the model is able to fit the experimental data as shown in Figure 1.

4.2 Kinetic Results

The dynamic behavior of the same hydrogel was also recorded. Initially, the gel was equilibrated in a buffer solution of pH = 3.0. The solution was then flushed and replaced with a solution of pH = 6.0. In the presence of the new solution, the gel began to swell towards its new equilibrium diameter. Measurements of the gel's diameter were taken during the course of the experiment using a Sony CCD camera. The experiment was stopped after the gel reached its equilibrium hydration. Deswelling experiments were performed by returning the bath solution to a pH of 3.0 and recording the gel's diameter at various times. Three separate swelling and deswelling experiments were performed.

The microchannel restricts the hydrogel from expanding in height direction and only allows swelling in the radial direction. This constraint allows swelling and

Table 2: Cylindrical hydrogel properties

\bar{D}_H	$9.3 \times 10^{-9} \frac{m^2}{s}$	K	$10^{-2.1} \text{ mM}$
$\bar{D}_{H_2PO_4}$	$8.79 \times 10^{-10} \frac{m^2}{s}$	$K_{H_2PO_4}$	$6.2 \times 10^{-5} \text{ mM}$
$c_{m_0}^s$	1800 mM	d_0	$300 \mu\text{m}$

deswelling to be modeled as a one-dimensional diffusion problem along the hydrogel's diameter as shown in Figure 2. Every point in the distribution used to model the cylinder has a corresponding value for \bar{c}_H and H . Numerical swelling simulations were started by setting all points in the gel in equilibrium with a solution of $\text{pH} = 3$. Using Donnan partitioning theory, initial concentrations inside the gel can be computed. The hydration values for the given solution pH are taken from Figure 1. At time t_1 , the solution bath was increased to $\text{pH} = 6$, and H and \bar{c}_H values at the boundary were adjusted to reflect equilibrium with the new solution. A normalized version of equation (12) was incremented in time according to the algorithm given in [10]. Hydration was considered to be constant over a single time step. After finding \bar{c}_H^{t+1} , H^{t+1} can be updated using equilibrium data. Deswelling simulations were conducted in the same manner, except the solution was initially at $\text{pH} = 6$ and changed to $\text{pH} = 3$. Numerical swelling/deswelling was also performed in the absence of buffer (i.e. $c_T = 0$). The results show the dramatic effect buffers can have on gel kinetics. Comparisons between numerical swelling and deswelling and experimental results are given in Figures 3 and 4.

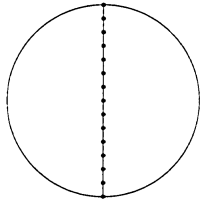


Figure 2: One-dimensional model of cylindrical hydrogel

5 CONCLUSION

The Finite Cloud Method has been applied to solve a partial differential equation describing the dynamic swelling and deswelling of ionic hydrogels. By including the buffer's effect on hydrogel kinetics, the model was able to match experimental results. Solution to the governing equation was obtained without generating a mesh to discretize the problem domain. Equilibrium data for pH induced swelling was matched using a thermodynamic model.

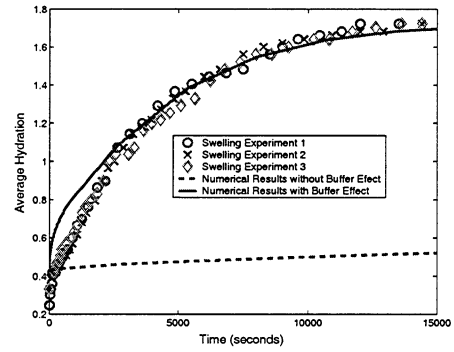


Figure 3: Numerical and experimental swelling

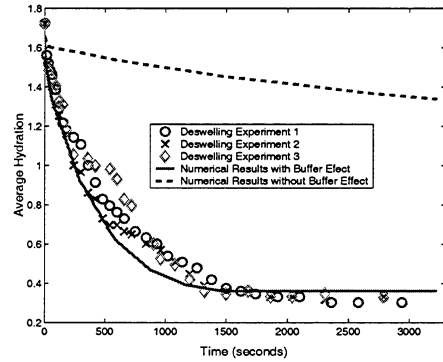


Figure 4: Numerical and experimental deswelling

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